

In the Claims

1-51 (Canceled)

52 (New). An isolated polypeptide antagonist of CXCR3-binding CXC chemokines, said antagonist comprising a mutant of CXCL11 in which:

a) at least one of the following basic residues of, numbered on the sequence of human mature CXCL11, is substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutamic Acid, Glutamine, Aspartic Acid, or Asparagine: 46, 62, or 70;

b) at least one of the following basic residues of, numbered on the sequence of human mature CXCL11, is substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutamic Acid, Aspartic Acid, or Asparagine: 46, 62, 66 or 70;

c) at least one of the following basic residues, numbered on the sequence of human mature CXCL11, is substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutamic Acid, Glutamine, Aspartic Acid, or Asparagine: 46, 62, 66, or 70 and at least one of the following basic residues, numbered on the sequence of human mature CXCL11, is additionally substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutamic Acid, Glutamine, Aspartic Acid, or Asparagine: 49, 52, 57, 59, or 71;

d) at least one of the following basic residues, numbered on the sequence of human mature CXCL11, is substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutamic Acid, Glutamine, Aspartic Acid, or Asparagine: 46, 62, 66, or 70 and at least one of the following basic residues, numbered on the sequence of human mature CXCL11, is additionally substituted to Glycine, Serine, Threonine, Proline, Glutamic Acid, Glutamine, Aspartic Acid, or Asparagine: 49, 52, 57, 59, 67 or 71;

e) one of the following combinations of basic residues, numbered on the sequence of human mature CXCL11, is substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutamic Acid, Glutamine, Aspartic Acid, or Asparagine:

i) 46, together with residue 49; residue 52; or residues 49 and 52;

ii) 62, together with residue 57; residue 59; or residues 57 and 59;

- iii) 66 and 70, together with residue 67; residue 71; or residues 67 and 71; or
- iv) 62 and 66, together with one or more of the following residues: 57, 59, 67, 70,

or 71;

f) at least one of the following basic residues, numbered on the sequence of human mature CXCL11, of an antagonist set forth in a), b), c) or d) is additionally substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutamic Acid, Glutamine, Aspartic Acid, or Asparagine: 5, 6, 8, 17, 20, 26 or 38;

g) the basic residues of an antagonist as set forth in a), b), c), d), e) or f) is substituted with Alanine or Glycine;

h) said antagonist comprises CXCL11-2B3 (SEQ ID NO: 3), CXCL11-3B3 (SEQ ID NO: 4), or CXCL11-4B4 (SEQ ID NO: 5);

i) one or more of the first nine amino acids in the amino-terminal domain of the human mature CXCR3-binding CXC chemokine have been added, deleted, or substituted in an antagonist as set forth in a), b), c), d), e), f), g) or h); or

j) one or more amino acids have been mutated to decrease the aggregation properties of an antagonist as set forth in a), b), c), d), e), f), g), h) or i).

53 (New). The isolated polypeptide antagonist according to claim 52, wherein at least one of the following basic residues of, numbered on the sequence of human mature CXCL11, is substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutamic Acid, Glutamine, Aspartic Acid, or Asparagine: 46, 62, or 70.

54 (New). The isolated polypeptide antagonist according to claim 52, wherein at least one of the following basic residues of, numbered on the sequence of human mature CXCL11, is substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutamic Acid, Aspartic Acid, or Asparagine: 46, 62, 66 or 70.

55 (new). The isolated polypeptide antagonist according to claim 52, wherein at least one of the following basic residues, numbered on the sequence of human mature CXCL11, is

substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutamic Acid, Glutamine, Aspartic Acid, or Asparagine: 46, 62, 66, or 70 and at least one of the following basic residues, numbered on the sequence of human mature CXCL11, is additionally substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutamic Acid, Glutamine, Aspartic Acid, or Asparagine: 49, 52, 57, 59, or 71.

56 (New). The isolated polypeptide antagonist according to claim 52, wherein at least one of the following basic residues, numbered on the sequence of human mature CXCL11, is substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutamic Acid, Glutamine, Aspartic Acid, or Asparagine: 46, 62, 66, or 70 and at least one of the following basic residues, numbered on the sequence of human mature CXCL11, is additionally substituted to Glycine, Serine, Threonine, Proline, Glutamic Acid, Glutamine, Aspartic Acid, or Asparagine: 49, 52, 57, 59, 67 or 71.

57 (New). The isolated polypeptide antagonist according to claim 52, wherein one of the following combinations of basic residues, numbered on the sequence of human mature CXCL11, is substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutamic Acid, Glutamine, Aspartic Acid, or Asparagine: 46, together with residue 49; residue 52; or residues 49 and 52.

58 (New). The isolated polypeptide antagonist according to claim 52, wherein one of the following combinations of basic residues, numbered on the sequence of human mature CXCL11, is substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutamic Acid, Glutamine, Aspartic Acid, or Asparagine: 62, together with residue 57; residue 59; or residues 57 and 59.

59 (New). The isolated polypeptide antagonist according to claim 52, wherein one of the following combinations of basic residues, numbered on the sequence of human mature CXCL11, is substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutamic Acid, Glutamine, Aspartic Acid, or Asparagine: 66 and 70, together with residue 67; residue 71; or residues 67 and 71; or

60 (New). The isolated polypeptide antagonist according to claim 52, wherein one of the following combinations of basic residues, numbered on the sequence of human mature CXCL11, is

substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutamic Acid, Glutamine, Aspartic Acid, or Asparagine: 62 and 66, together with one or more of the following residues: 57, 59, 67, 70, or 71.

61 (New). The isolated polypeptide antagonist according to claim 52, wherein one of the following combinations of basic residues, numbered on the sequence of human mature CXCL11, is substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutamic Acid, Glutamine, Aspartic Acid, or Asparagine: 66 and 70, together with residue 67; residue 71; or residues 67 and 71; or

62 (New). The isolated polypeptide antagonist according to claim 52, wherein at least one of the following basic residues, numbered on the sequence of human mature CXCL11, of an antagonist set forth in a), b), c) or d) is additionally substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutamic Acid, Glutamine, Aspartic Acid, or Asparagine: 5, 6, 8, 17, 20, 26 or 38.

63 (New). The isolated polypeptide antagonist according to claim 52, wherein the basic residues of an antagonist as set forth in a), b), c), d), e) or f) is substituted with Alanine or Glycine.

64 (New). The isolated polypeptide antagonist according to claim 52, wherein said antagonist comprises CXCL11-2B3 (SEQ ID NO: 3), CXCL11-3B3 (SEQ ID NO: 4), or CXCL11-4B4 (SEQ ID NO: 5).

65 (New). The isolated polypeptide antagonist according to claim 52, wherein one or more of the first nine amino acids in the amino-terminal domain of the human mature CXCR3-binding CXC chemokine have been added, deleted, or substituted in an antagonist as set forth in a), b), c), d), e), f), g) or h).

66 (New). The isolated polypeptide antagonist according to claim 52, wherein one or more amino acids have been mutated to decrease the aggregation properties of an antagonist as set forth in a), b), c), d), e), f), g), h) or i).

67 (New). The isolated polypeptide antagonist according to claim 52, further comprising:
a) an amino acid sequence belonging to a protein sequence other than the corresponding CXCR3-binding CXC chemokine; or b) a molecule to which said antagonist is complexed or conjugated.

68 (New). The isolated polypeptide antagonist according to claim 67, wherein said amino acid sequence is selected from one or more of these protein sequences: extracellular domains of membrane-bound protein, immunoglobulin constant region, multimerization domains, extracellular proteins, signal peptide-containing proteins, or export signal-containing proteins.

69 (New). The isolated polypeptide antagonist according to claim 67, wherein said antagonist is complexed or conjugated to a molecule chosen from radioactive labels, biotin, fluorescent labels, cytotoxic agents, or drug delivery agents.

70 (New). A composition comprising a pharmaceutically acceptable carrier and a carrier and a polypeptide antagonist according to claim 52.

71 (New). An isolated polynucleotide encoding a polypeptide according to claim 52.

72 (New). A vector comprising a polynucleotide encoding a polypeptide according to claim 52.

73 (New). An isolated host cell comprising a polynucleotide encoding an polypeptide according to claim 52.

74 (New). A method of making a polypeptide comprising culturing a host cell comprising a polynucleotide encoding an polypeptide according to claim 52 under conditions that allow for the expression of said polypeptide.

75 (New). The method according to claim 74, further comprising isolating said polypeptide.